The Impacts of Helicobacter Pylori Antigen Positivity on Ankylosing Spondylitis

Helicobacter Pylori Antijen Pozitivitesinin Ankilozan Spondilit Üzerine Etkileri

Helicobacter Pylori and Ankylosing Spondylitis

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Özet

Amaç: Biz Ankilozan Spondilit (AS) hastalık aktivitesi ve klinik bulguları üzerine Helicobacter pylori (H. Pylori) enfeksiyonunun etkilerini ortaya çıkarmayı amaçladık. Gereç ve Yöntem: Kırk-sekiz AS hastası bu çalışmaya dahil edildi. Hastaların, yaş, cinsiyet, hastalık ve medikasyon sürelerini de içeren demografik bilgileri kaydedildi. Laboratuvar analizi; eritrosit sedimentasyon hızı (ESH), C-reaktif protein (CRP) ve gaytada H. Pylori antijen tespitini içermekte idi. Hastalık aktivitesi, fonksiyonel ve klinik durum, sırasıyla Bath Ankilozan Spondilit Hastalık Aktivite indeksi (BASHAİ), Bath Ankilozan Spondilit Fonksiyonel indeksi (BASFİ) ve Bath Ankilozan Spondilit Metrolojik indeks (BASMİ) ile değerlendirildi. Hastaları, gaytada H. pylori antigen pozitifliğine gore, H. pylori pozitif ve negatif hastalar olmak üzere ikiye ayırdık. Bulgular: Hastaların ortalama yaşı 41.9+11.8 idi. Gaytada H. pylori pozitif olan hastalarda, negatif olan hastalara kıyasla, CRP düzeyleri hafifçe fakat anlamlı olmadan yüksekti (p=0.08). H. pylori negatif ve pozitif olan hastalar kıyaslandığında, ESH düzeyleri, BASHAİ, BASFİ ve BASMİ skorları açısından anlamlı bir farklılık bulunamadı (p-değerleri hepsi için >0.05). Regresyon modelinde, BASHAİ skorları ile H. pylori antigen pozitifliği, ESR ve CRP düzeyleri arasında bir etkileşim bulunamamıştır (p-değerleri hepsi için >0.05). Tartışma: H. pylori enfeksiyonu, AS hastalık aktivitesinde muhtemel etkileri varmış gibi görünmektedir. Bu durumu aydınlatmak için, daha büyük hasta populasyonlu ve daha uzun sureli çalışmalar tavsiye edilir.

Anahtar Kelimeler

Ankilozan Spondilit; Helicobacter Pylori; Hastalık Aktivitesi; BASHAİ

Abstract

Aim: We aimed to clarify the impacts of H. pylori infection on disease activity and clinical findings of AS. Material and Method: Forty-eight patients with AS were included in this study. The demographic data including age, sex, durations of the disease and medication of the patients were recorded. The laboratory analysis comprised Erythrocyte sedimentation rate (ESR), C-reactive protein (CRP) and H. pylori antigen determination in gaita. The disease activity, functional disability and clinical status were assessed using the Bath Ankylosing Spondylitis Disease Activity Index (BASDAI), The Bath Ankylosing Spondylitis Functional index (BASFI) and The Bath Ankylosing Spondylitis Metrology Index (BASMI) respectively. We divided patients according to H. pylori antigen positivity in gaita as H. pylori positive and negative patients. Results: The mean age of patients was 41.9+11.8. CRP levels were slightly but not significantly higher in patients with positive H. pylori antigen compared to those in patients without H. pylori antigen in gaita (p=0.08). There was no significant difference in terms of ESR levels, BASDAI, BASFI and BASMI scores in patients with positive H. pylori antigen compared to those in patients with negative H. pylori antigen in gaita (p-values were >0.05 for all). In regression model BASDAI score was found to have no relationship with H. pylori antigen positivity, ESR and CRP levels (p-values were >0.05 for all). Discussion: H. pylori seemed to have probable impacts on the disease activity of AS. Studies with greater patient population and longer follow-up periods are warranted to enlighten this issue.

Keywords

Ankylosing Spondylitis; Helicobacter Pylori; Disease Activity; BASDAI

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Introduction

Ankylosing spondylitis (AS) is a chronic inflammatory systemic disease of unknown origin which affects the axial skeleton and peripheral joints [1]. Genetic tendency and a number of infectious agents such as Klebsiella pneumonia are the main subjects which are accused in the pathogenesis of AS [2, 3]. On the other hand, besides a lot of objective parameters which were supported to evaluate disease activity in AS [4-6], the gold standard currently used today is the Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) which includes subjective measurements of the patients and clinicians [7].

The role of infections in autoimmune diseases was investigated before and gram negative bacteria such as Yersinia, Salmonella and Shigella as well as the organism Chlamydia trachomatis were found to be associated with the development of reactive arthritis [8]. Helicobacter pylori (H. pylori) infection was also found to reveal a number of host immune responses which results in chronic inflammation [9]. The protective role of H. pylori infection on some autoimmune chronic inflammatory diseases such as inflammatory bowel disease was also reported [10]. Besides, H. pylori infection was found to take part in the pathogenesis of Rheumatoid arthritis (RA) [11]. Furthermore, eradication of H. pylori was supported to induce a significant improvement in the disease activity of several chronic inflammatory diseases including RA [12] and chronic idiopathic urticaria [13]. However the relationships between H. pylori infection and disease activity and functional status in patients with AS have not been fully understood yet. Therefore we aimed to clarify the impacts of H. pylori infection on disease activity and severity of AS.

Material and Method

Forty-eight patients with AS (female 15, male 33) who fulfilled the Modified New York criteria [14] were included in this study from our outpatient clinic. Informed consents of the patients were obtained before enrolling in this study. The demographic data including age, sex, durations of disease and medication of patients were recorded. All of the patients were using one of non-steroidal anti-inflammatory drugs and/or sulphasalazine 2-3gr/day and/or biologic agents. The patients having concomitant another concomitant rheumatic disease were excluded from the study.

The laboratory analysis comprised Erythrocyte sedimentation rate (ESR), C-reactive protein (CRP) and H. pylori antigen determination in gaita. ESR was measured by spectrophotometric assay (Alifax Test - 1 THL, 950 nm). CRP was determined by turbidimetric method (TOSHIBA ACCUTE /TBA-40FR). The stool assay was performed using the H.pylori Antigen Test (DIA. PRO, Milano, Italy). This test kit is a rapid, visual immunochromatographic test for the qualitative detection of H. pylori antigen in human fecal samples. A positive result suggests the presence of H.pylori antigen in fecal specimens.

Visual analog scale (VAS) was used to evaluate patient's global assessment and physician's global assessment of the illness (0-10 cm, 0=no pain and 10=severe pain).

The disease activity was assessed by using the Turkish version of BASDAI. BASDAI is a self-administered questionnaire consisting of six questions relating to five major symptoms including fatigue, spinal pain, joint pain/swelling, areas of localized tenderness, and morning stiffness. Morning stiffness was measured in terms of both severity and duration. In each of five questions, the patients were asked to rate the degree of pain or stiffness they felt over the previous week on a 10 cm horizontal VAS, while the scale for duration of morning stiffness is graded every 15 minutes in 0-2 hours. The mean of two scores of morning stiffness is calculated. VAS has no distinguishing marks except the words 'easy' and 'impossible' at either ends of the line to indicate the direction of severity. Total BASDAI score is the mean of the total of five scores with higher scores indicating higher disease activity [7].

Functional disability was evaluated using the Turkish version of Bath Ankylosing Spondylitis Functional index (BASFI). BASFI consists of eight questions on daily activities and two additional questions to assess patients' ability to cope with everyday life. Each question was answered on 0-10 cm horizontal VAS reflecting status over previous month. The VAS have no distinguishing marks except the words 'easy' and 'impossible' at either ends of the line to indicate the direction of severity. BASFI score is the mean of the total of ten scores, with higher scores indicating more severe impairment [15].

Clinical status was evaluated with Bath Ankylosing Spondylitis Metrology Index (BASMI). BASMI was calculated with the measurements of wall to tragus distance, lumbar flexion, cervical rotation, lumbar lateral flexion, and intermalleolar distance. Lateral flexion of lumbar spine was measured bilaterally and the mean of right and left flexion values were accepted as a single value. Each measurement received either 0 (mild disease involvement), 1 (moderate disease involvement), or 2 (severe disease involvement) points. The sum of five scores is 0-10 with higher scores indicating higher disease involvement [16].

We divided patients according to H. pylori antigen positivity in gaita as H. pylori positive and negative patients.

Data were analyzed using the Statistical Package for Social Sciences (SPSS) software version 15.0 for Windows (SPSS Inc., Chicago, IL). Frequencies and percentages were used for categorical data. For comparison of quantitative variables, suitability of parametric test conditions was checked. For variables which met parametric test conditions, Student's t test and for other variables Mann-Whitney U test were used for two group comparisons. For evaluation of categorical variables, chi-square (X2) test was used. To determine independent predictors of BASDAI score, linear regression analysis with enter method was performed. $P<0.05$ is accepted to be significant.

Results

The mean age of patients was 41.9+11.8. Fifteen of patients were female and the others were male. The demographic, clinical and laboratory findings of the patients were summarized in table 1.

CRP levels were slightly but not significantly higher in patients with positive H. pylori antigen compared to those in patients without H. pylori antigen in gaita ($p=0.08$). There was no significant difference in terms of ESR levels, BASDAI, BASFI and BASMI scores in patients with positive H. pylori antigen compared to those in patients with negative H. pylori antigen in gaita (p values were >0.05 for all). These were shown in table 2.

In order to find out the possible independent predictors of BAS-

Table 1. The laboratory and clinical characteristics of the patients with AS (n=48)

	Mean+SD	Min-max
Age (year)	41.9+11.8	22-70
Gender (female/male)	15/33	
H. pylori antigen (positive/negative)	12/36	
Duration of the disease (month)	86.4+78.1	1-336
Duration since start of medication (month)	81.1+70.2	1-264
ESR (mm/h)	29.2+23.0	2-90
CRP (mg/L)	11.8+13.3	1-66
VAS patient's global assessment	5.0+2.2	1-9
VAS physician's global assessment	4.8+2.1	1-9
BASDAI	3.5+1.8	0.4-7.2
BASMI	2.4+2.2	0-8
BASFI	2.3+1.8	0-6.3

mean+SD: mean+standard deviation, min-max: minimum-maximum, AS: Ankylosing Spondylitis, H. pylori: Helicobacter pylori, ESR: Erythrocyte sedimentation rate, CRP: C-reactive protein, VAS: Visual analog scale, BASDAI: Bath Ankylosing Spondylitis Disease Activity Index, BASMI: Bath Ankylosing Spondylitis Metrology Index, BASFI: Bath Ankylosing Spondylitis Functional Index.

Table 2. The laboratory and clinical characteristics of the patients with AS (n=48) according to H. pylori antigen positivity

	H. pylori antigen (+) (n=12)	H. pylori antigen (-) (n=36)	p
Age (year)	45.1+11.8	40.1+11.2	0.29
Gender (female/male)	5 / 7	10 / 26	0.37
Duration of the disease (month)	70.8+70.0	91.6+80.9	0.43
Duration since start of medication (month)	69.0+71.6	85.1+70.3	0.50
ESR (mm/h)	24.8+21.5	30.7+23.6	0.45
CRP (mg/L)	6.3+7.5	13.7+14.4	0.08
VAS patient's global assessment	4.5+2.4	5.2+2.1	0.34
VAS physician's global assessment	4.2+2.1	5.0+2.1	0.24
BASDAI	3.4+1.7	3.5+1.9	0.45
BASMI	2.6+3.2	2.3+1.8	0.69
BASFI	2.0+1.7	2.5+1.8	0.53

mean+SD: mean+standard deviation, AS: Ankylosing Spondylitis, H. pylori: Helicobacter pylori, ESR: Erythrocyte sedimentation rate, CRP: C-reactive protein, VAS: Visual analog scale, BASDAI: Bath Ankylosing Spondylitis Disease Activity Index, BASMI: Bath Ankylosing Spondylitis Metrology Index, BASFI: Bath Ankylosing Spondylitis Functional Index, $p<0.05$ is significant.

DAI score, we have performed linear regression analysis. In regression model BASDAI score was taken as dependent variable and H. pylori antigen positivity, ESR and CRP levels were taken as independent variables. Regression model with enter method revealed no significant relation between these independent variables and BASDAI scores (p values were >0.05 for all) (Table 3).

Table 3. Lineer regression analysis of BASDAI scores with ESR, CRP and H. pylori antigen positivity in patients with AS.

	Beta	p	CI
ESR (mm/h)	0.168	0.38	-0.017-0.043
CRP (mg/L)	0.052	0.79	-0.046-0.060
H. pylori antigen positivity	0.002	0.99	-1.257-1.276

BASDAI: Bath Ankylosing Spondylitis Disease Activity Index, ESR: Erythrocyte sedimentation rate, CRP: C-reactive protein, H. pylori: Helicobacter pylori, AS: Ankylosing Spondylitis.

Discussion

In the present study, we have found that there were slightly but not significantly higher levels of CRP in patients with positive H. pylori antigen compared to patients with negative H. pylori antigen.

So far, conflicting results about the role of infectious diseases in the pathogenesis and severity of several rheumatic diseases were reported in the literature [8-11, 17]. H. pylori was investigated whether it is related with several autoimmune diseases or not and it was found to be associated with development and severity of Sjögren's syndrome, Systemic sclerosis and Psoriasis while no relation was found with RA, Systemic lupus erythematosus, vasculitides, chronic urticaria, Immune thrombocytopenic purpura and Hashimoto's thyroiditis [17]. On the other hand, several studies indicated H. pylori as a potential protective agent against Multiple Sclerosis [18, 19]. However, the impacts of H. pylori infection on disease severity and clinical findings of AS has not been fully clarified yet.

Previously, H. pylori infected RA patients showed a progressive improvement both in disease activity and laboratory parameters with eradication of H. pylori compared to H. pylori negative patients. In these studies, CRP levels were similar both in H. pylori negative and positive patients at the baseline, but after eradication of H. pylori, it had progressively decreased in RA patients who were H. pylori positive [11, 12]. Conversely, no relation between disease activity of RA and eradication of H. pylori was also reported [20]. In the same way, we have observed slightly but not significantly higher CRP levels in AS patients who were H. pylori positive. This discrepancy may be due to different associations between diseases and CRP as well as various treatment methods of patients.

Several parameters had been investigated whether they have impacts on disease activity of AS or not in order to find out an objective laboratory marker in evaluating disease activity of AS [1, 4-6]. For the same purpose, we have used linear regression analysis to clarify the parameters affecting BASDAI, the disease activity index of AS, and we did not find any contributions of the parameters on BASDAI score in this study.

The present study has several limitations. Relatively smaller number of study population is one of them, since we have found slightly but not significantly higher levels of CRP in patients with positive H. Pylori antigen compared to those in patients with negative H. Pylori antigen. With a relatively larger patient population this result may reach a significant level. We have studied H. pylori antigen in gaita, but the studies in literature mostly measured the antigen of H. pylori in serum. The cross sectional design might have caused false negative and positive results and could not have clarified the relations precisely.

In the present study, we have found slightly but not significantly higher levels of CRP in patients who were H. pylori positive, compared to those in H. pylori negative patients. In conclusion, H. pylori seemed to have possible impacts on the disease activity of AS. Studies with greater patient population and longer follow-up periods are warranted to enlighten this issue.

Competing interests

The authors declare that they have no competing interests.

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